Vol. 75 June 1958 No. 6

ARCHIVES OF PEDIATRICS

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Progressive Lipodystrophy following Infection — *Edward L. Brown, M.D.*

Scorpion Poisoning and its Treatment in Egyptian Children — *S. Awwaad, M.D., D.C.h.*

Physical Fitness of School Children — *Herman Robbins, M.D.*

Treatment of Upper Respiratory Infections in Children — *Lester A. Nathan, M.D.*

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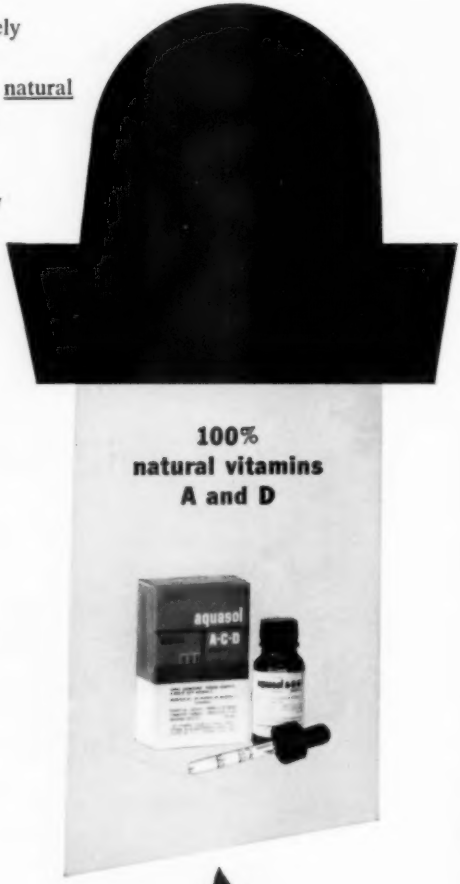

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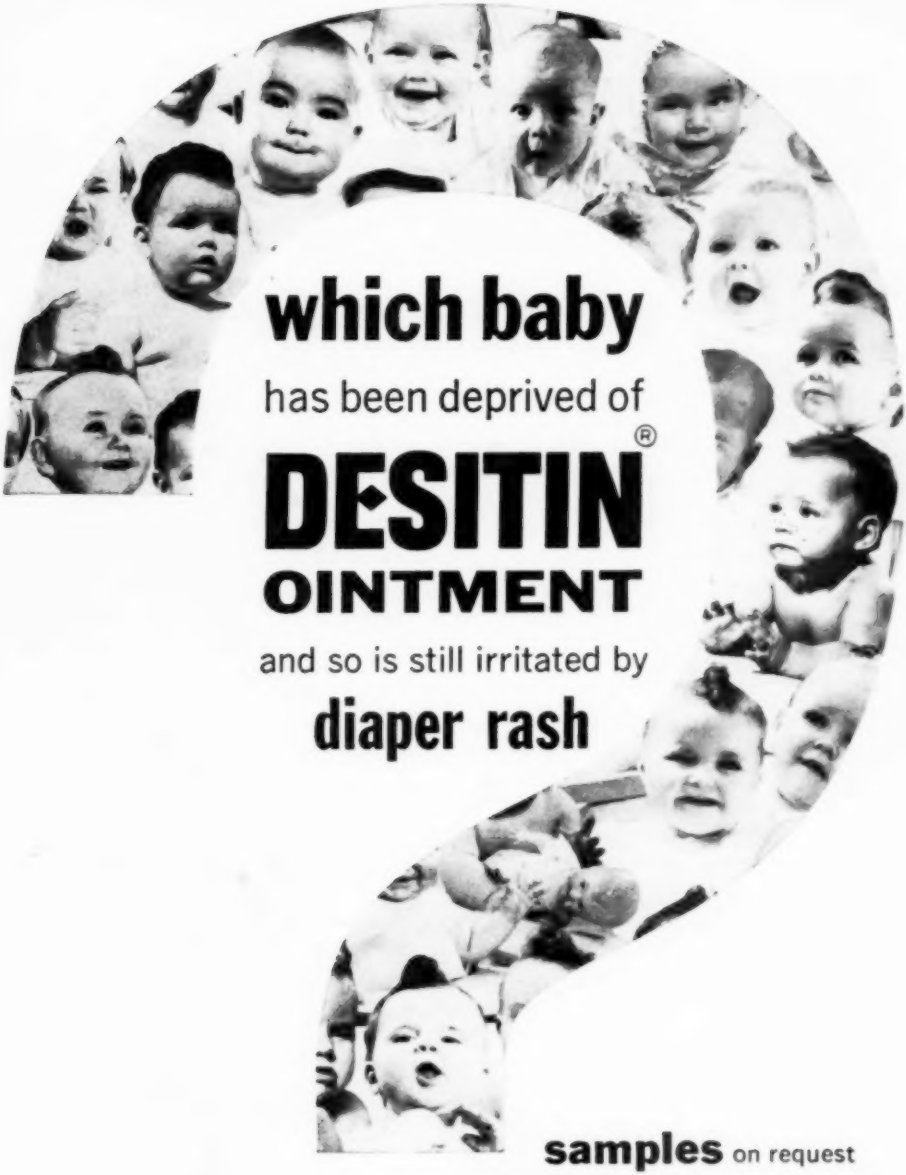

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CONTENTS

ORIGINAL ARTICLES

Progressive Lipodystrophy Following Infection — Report of Three Cases
Edward E. Brown, M.D., F.A.A.P. 227

Clinical Studies on Scorpion Poisoning and Its Treatment in Egyptian Children
S. Awwaad, M.D., D.Ch. 234

Physical Fitness of School Children in the United States
Herman Robbins, M.D., F.A.C.C. 245

Use of Glucosamine-Potentiated Tetracycline* in the Treatment of Upper Respiratory Infections in Children
Lester A. Nathan, M.D. 251

Hemorrhagic Complications of Measles
Nizamettin Kilic, M.D. 266

SPECIAL ARTICLE

An Evaluation of Uric Acid as an Etiological Factor in some of the Obscure Pathologies
Herman C. Amster, Ph.G. 256

ABSTRACTS

Organic and Organizational Aspects of School Adjustment Problems
H. F. Weir, M.D. — R. L. Anderson, M.D. 269

Poliomyelitis in the Child under a Year of Age
E. Sujov, M.D. — G. Halbertstein, M.D. 269

Brand Name Drugs*

Henry A. Davidson, M.D.

More than 85 per cent of all prescriptions are prefabricated by the pharmaceutical manufacturer. They are not compounded by the retail druggist. Thus the integrity of the manufacturer becomes as important today as the honesty and cleanliness of the retail pharmacist was in 1900. Modern mass production, whatever its disadvantages, does guarantee standardization. One spoonful of a good brand's Elixir XYZ has the same composition and potency as another teaspoonful of the same brand's Elixir (if you use the same teaspoon). This is not true of a fly-by-night manufacturer of shoddy merchandise. But it is true of any of the reputable manufacturers who advertise in this and other physician-controlled journals.

Control is the secret of sound manufacture—control of purity, viscosity, solubility, potency, vehicle and particle size. To exercise control at every step of the manufacturing process is expensive. A manufacturer who ignores controls can sell his product cheaper. It may be announced as a "pharmaceutic equivalent"—but it isn't, even though it looks like an equivalent in color of fluid or shape of tablet.

Fluids separate, tablets decompose, ointments can deteriorate and any medication can become contaminated. The honorable manufacturer determines the "shelf-life" of a product and advises the retailer, or marks an expiration date. This kind of determination is expensive. By stamping on an expiration date, the manufacturer stands to lose some sales. The third-grade maker avoids that danger. He doesn't determine shelf-life, or he stamps no accurate expiration date on the package. So he can sell his product at a bargain. Of course, the aspirin tablet may deteriorate and give the odor of acetic acid. Still, it's a bargain.

One of the oddities of the drug trade is that the manufacturer spends a fortune on research, and counts himself lucky to get one usable product out of fifty experiments. He pours down the drain the cost of the other 49 projects. His purpose, to be sure, is not charitable. He expects it to pay off, hoping to make enough profit on the one successful experiment to pay the workers on the 49 wild goose chases. Still, if an unethical manufacturer can borrow the results of that research, he can undercut the original maker in price; the second company doesn't have to pick up the research tab.

* Editorial reprinted from the January 1958 issue of the Journal of the Medical Society of New Jersey (Trenton).

Hence, the by-passing of good brand-named products is a body blow to research. Why should a company spend millions in research to see their final products left on the shelf in favor of a cheaper substitute?

Chemically speaking, one antacid tablet may be the same as the other. Still, if you are chewing the tablet, you prefer the one with a smooth taste; and if you prefer the brand-named, more elegant tablet, your patient is entitled to it too.

A suppository that melts in the container before use—or fails to melt in the body cavity during use—is worthless no matter how cheaply it can be bought. Melting point control requires expensive equipment, and adds to the retail price. A first-class manufacturer, however, will not put out a suppository without a controlled melting point. A third rate manufacturer may, and sell it cheaper.

So the experienced physician is not defensive about prescribing brand-named products—or giving the retail pharmacist a choice of reliable brand names. He knows that the patient can buy an ersatz product a little cheaper. But precious things don't sell at cut-rate prices.

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ARCHIVES OF PEDIATRICS

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PROGRESSIVE LIPODYSTROPHY FOLLOWING INFECTION

Report of Three Cases

EDWARD E. BROWN, M.D., F.A.A.P.
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Lipodystrophy is an enigmatic disease showing a progressive, segmental loss of fat, usually in the face and upper portion of the body. In 1956, Jones[1] estimated the total number of recorded cases was 206. Undoubtedly, many borderline cases exist and others have been overlooked.[2, 3]

There are three unexplained peculiarities in lipodystrophy: (1). highest incidence at ages six to eight;[4-7] (2). localized absence of subcutaneous fat and fat cells;[8] (3). frequent association of such atrophy with hypertrophy of fat elsewhere.[8-11]

ETIOLOGY

The cause of lipodystrophy is unknown. The various theories of causation include (a) endocrine dysfunction; (b) disturbances of autonomic innervation and trophic changes; and (c) infection.

Systemic infection is the most common antecedent of progressive lipodystrophy. Weir Mitchell[12] in 1885 described the first case, that of a twelve year old girl, whose loss of fat followed severe cold with cough and expectoration which lasted for three months at the age of five. Subsequently, many writers emphasized the role of infection.[2, 3, 5, 7, 9, 13-18] Preceding infections included measles,[19] diphtheria, pertussis (Garrahan, 1920), pneumonia, influenza,[20] rheumatic fever,[3] sinusitis,[7, 14] otitis and mastoiditis,[3] erysipelas[9] and encephalitis.[21, 22] Pollack[23] considered basal meningitis or hydrocephalus as one of the underlying causes. Brain[24] ascribed lipodystrophy to disturbances of autonomic innervation possibly due to infection. Hartston[18] said that the onset often followed acute specific fever. Parmalee[25] stated that in twenty-three out of ninety-five cases the onset followed an acute infection.

In two of three cases reported by Baxter and his co-workers,[3] infection preceded. Sometimes the initial infection is overlooked but a later infection may produce further loss of fat. Baxter described a case starting in the early teens, but "at the age of 20 years the patient suffered from an attack of quinsy, complicated by severe septic throat and mastoiditis. Following this illness the thinness of the upper part of the body became more pronounced."

Thyroiditis may precede lipodystrophy. Thyroid dysfunction varying from hyperplasia of the gland to thyrotoxicosis was found by Murray (1952) to be present in sixteen out of twenty-one cases. That thyrotoxicosis may be infectious is suspected from the frequency with which it follows thyroiditis,[26] itself a sequel of many types of acute infection.[27]

In some seven cases of lipodystrophy under my observation, three of which are presented, chronic systemic infections were present. These three patients all had frequent colds, recurring morning headaches and were mouth-breathers, prominent symptoms of sinusitis.[28] All showed sinus tenderness upon palpation. The existence of sinusitis is suggested in cases described by Reuben[7] and Herrman[28] with headache and joint pain, and in cases which follow recurrent or persistent upper respiratory infections.

The *streptococcus* or its *toxin* may be an incitant of lipodystrophy. This is inferred (1) from the history of a preceding streptococcic infection and (2) from the age group involved. Both points are discussed briefly.

Preceding streptococcic infection. Several presumably streptococcic diseases are reported as preceding the onset of lipodystrophy. They include rheumatic fever, rheumatoid polyarthritis,[22] hematuria and sinusitis,[14] pyuria and tonsillitis,[11] quinsy, pharyngitis and mastoiditis.[3] In our three cases active chronic sinusitis may have been responsible for the progression of lipodystrophy.

Age group in lipodystrophy. Suggestive of streptococcic (rheumatic) causation of lipodystrophy is the age group involved. The peak ages of incidence of rheumatic fever[30] and lipodystrophy correspond exactly, namely, six to eight years.

Locus of involvement. Although no lesion has been demonstrated, the view is gaining ground that there is involvement of a possible center concerned with segmental fat metabolism.[13, 31] Parmalee,[25] Ivy[16] and Crosfill[2] would localize the lesion in the hypothalamic area. Parmalee writes: "The fact that one finds

marked disturbances in metabolism following encephalitis, a disease which seems to have its origin in the upper respiratory tract and which often results in obesity or other changes in the fat metabolism, and that an association exists between lipodystrophy and infection of the upper respiratory tract which might produce changes in the hypothalamic portion of the midbrain and disturbances of the vegetative nervous system, seems worthy of consideration." Crosfill believes that infections, common in childhood, "might produce a local encephalitis, with sequelae manifested by the dysfunction of appropriate nuclei."

CASE REPORTS

Three cases of lipodystrophy under my care follow:

Case 1. Girl, aged 10, (Fig. 1) started to show hollowness in cheeks when five years old, soon after removal of tonsils and adenoids. In the past year there was noted a further loss of fat in shoulder girdles and upper arms. She had frequent colds both before and after tonsillectomy. Since age 6, headaches were common, especially in the morning. She was always a mouth-breather.

Fig. 1. Age 10. Note hollowing of cheeks.

Physical examination reveals a well developed girl except for hollowness of cheeks, and loss of subcutaneous fat, also in upper arms, shoulders, and neck. The subcutaneous fat is diminished in the orbits causing the eyeballs to recede. The ethmoid and maxillary sinuses are tender; a postnasal mucopurulent discharge is present.

Diagnosis: Lipodystrophy; chronic sinusitis.

Case 2. Girl, aged 6 (Fig. 2), showed a recent hollowing of cheeks.

Fig. 2. Early lipodystrophy in girl aged 6 (Case 2). Beginning loss of fat only in upper part of body. Dark circles and puffs under eyes are caused by sinusitis. Note loss of fat in cheeks.

History revealed frequent colds, mouth-breathing, sniffing in the absence of a known cold, occasional headaches, and possible pyelonephritis.

Physical examination: Child appears older than age six; cheeks are sunken, frontal bossae are prominent; pallor is moderate; circles under eyes; nasal obstruction slight. Sinus, tenderness: ethmoids +++; antra ++. Cervical, submaxillary, axillary and shotty inguinal adenitis all present. Patient sniffs at intervals. Abdomen slightly distended. Height: 43½ inches; weight: 40 pounds; pulse varies from 96 to 120; temperature 100° F.

Laboratory data: Mantoux slightly positive. R.B.C. 3,020,000; hemoglobin 55 per cent; W.B.C. 15,900; 54 per cent neutrophils. Urine: albumin +++; r.b.c. 10, w.b.c. 30 per h.p.f.; occasional hyaline and cellular cast.

X-ray lungs: Tracheo-bronchial adenitis, more prominent on right with possible chronic mediastinitis.

Diagnosis: Early lipodystrophy; chronic sinusitis; pyelonephritis; secondary anemia; generalized lymphadenitis.

Case 3. Boy, aged 10, showed hollowing of cheeks since age 7; there was also some loss of fat in neck and shoulders (Fig. 3).

History is one of frequent colds and tonsillitis, for which an

adenotonsilliectomy was done at age 7. He frequently complains of abdominal pain,[32] morning headaches; he is a mouth-breather and is becoming deaf.

Fig. 3. Age 10. Constant mouth-breathing and photophobia are secondary to chronic sinusitis.

Physical examination reveals marked hollowing of cheeks, making him appear older than his age. Height is 55 inches; weight, 74 pounds. Subcutaneous fat is absent in neck, thus permitting easy palpation of the styloid processes. One notes photophobia, blepharitis, mouth-breathing, nasal obstruction, nasal twang, tenderness of ethmoids and antra, gingivitis and cervical adenitis. He hears with difficulty.

Diagnosis. Lipodystrophy; chronic sinusitis; gingivitis; progressive deafness.

DISCUSSION

When a self-limiting disease like influenza, measles, pertussis or pneumonia is followed by any chronic disease, be it lipodystrophy, or arthritis, one should rule out a continuing insult.[33] The frequency with which chronic sinusitis complicates contagious diseases[33] may well explain the bacterial activity which continues for months or years beyond the short duration of the original disease.

Streptococcic toxin penetrates the sinus mucosa to enter the cervical lymphatics and thence to the main lymphatics and blood stream. The tissue response is then variable; depending on the tissues invaded, such toxins may produce rheumatic fever,[34] nephritis, acromegaly,[35] hypothyroidism,[36] hypoadrenia[37] hypoinsulinism (dia-

betes),[38] etc. Any or all tissues may be invaded. However, until the "fat center" is located and until lesions can be demonstrated in this center, the question of the cause of lipodystrophy must remain an open one.

CONCLUSIONS

Three cases of lipodystrophy associated with, and possibly caused by, active chronic sinusitis are presented.

Chronic streptococcic toxemia probably is the most frequent incitant of lipodystrophy.

The site of attack by toxins may be the hypothalamus. Further research is needed to establish whether in the hypothalamus there exists a center for controlling both the loss and deposition of fat in a segmentary fashion.

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SYNDROME OF THE ANTERIOR SPINAL ARTERY. B. Lindquist. (Acta paediat., 46:380-386, July 1957). The author reports on a 6-year-old boy with the classic syndrome of the anterior spinal artery including involvement of both the upper and the lower extremities. Paralysis developed within half an hour with tetraplegia followed by dissociated anesthesia and loss of bladder and bowel function. A striking feature of the clinical aspect of the patient was the acute and dramatic onset of symptoms. This suggested a vascular lesion as the cause of the syndrome, possibly because of trauma, since just before the onset the boy was playing in a barn by himself. The spread of the symptoms suggested that the lesion was located at the level of the lowermost cervical and uppermost thoracic segments of the spinal cord, where it involved mainly the anterior port of the medulla. The patient improved slowly. The gross functional power of the arms was good with the exception of the hands, the strength of which was severely impaired. Twelve months after the onset the patient was able to walk on crutches and for short distances with a walking stick only. Considerable improvement was noted in the function of the bladder and bowel, so that he had become continent. The lesions of the hands appeared to be irreversible and a certain degree of permanent invalidism must, therefore, be expected. This is apparently the first report of the classic syndrome of the anterior spinal artery in a child. —*J.A.M.A.*

CLINICAL STUDIES ON SCORPION POISONING AND ITS TREATMENT IN EGYPTIAN CHILDREN

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INTRODUCTION

Scorpions are insects belonging to the species of Arachnida, and they live in tropical and subtropical regions. They vary from one inch to eight inches in size and are armed with a sting at the end of a segmented tail. The sting consists of a vesicle containing a pair of poison glands and a sharp hollow spine through which the venom is injected into the victim. Scorpions thrive mainly on insects. Their poison varies in toxicity. It is noted that the fatalities from scorpion sting are for the most part limited to children and debilitated adults. It is also noticed that repeated stinging by the insect confers on the victim an immunity to its ill-effects. Such acquired immunity explains how vagrants in Upper Egypt, where scorpions are prevalent, can handle these insects and be stung by them without being affected.

Scorpions adapt themselves to diverse conditions, some thriving in tropical forests, some on open plains, and others in sandy deserts. However, they become active only during their mating period which occurs in the summer season, while in the other seasons of the year, they usually lead a solitary existence. They are nocturnal, becoming active during the night and concealing themselves through the day under rocks and stones, in burrows and in almost any natural crevice, and in Egypt, the palm tree is a favoured hiding place for them.

HISTORICAL REVIEW

Studies on the toxic effects of the venom have been carried out since ancient history. Galenus[1] (131-201 A.C.), stated that if the sting injected the venom into an artery, it caused rapid loss of consciousness; in a nerve, it caused convulsions; and in a vein, it caused gangrene. Avicenna[2] (Ibn Sina) (1412), mentioned salivation, lacrimation, sweating, shivering, vomiting, abdominal distension, edema of the tongue and trismus of the jaw among the chief symptoms of scorpion poisoning.

Among the leading investigators on this subject, the following authors may be mentioned: Redi[3] (1731) studied the effect of the

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sting on pigeons and on dogs. Mauperitus[4] (1731) noticed that in animals stung by the scorpion, tetanic spasms precede the occurrence of paralysis, Joyeux-Laffino[5] (1883) studied the venom from the chemical point of view. Bert[6] (1885) compared the effects of the venom on guinea-pigs, birds and dogs. He also made some comments on the post mortem changes in these animals. Kutoba[7] (1918) and Houssey[8] (1919) discussed the mode of action of the venom. Barros[9] (1939) studied the post mortem changes in rabbits killed with the venom.

In Egypt, important advances in that field were made by Wilson[10] (1904 and 1921) who described in detail the general effects of the venom on different animals, and discussed some of the properties of the active principle of the venom. A. H. Mohammed[11] (1937 and 1939) has applied himself to the study of the venom from the physiological, biochemical, immunological and spectroscopic points of view. A. Hassan and Z. Hassan[12] (1932) separated the pure toxin from the crude venom. A. Hassan and A. H. Mohammed[13] (1940) after repeated experimental work on animals recommended the administration of Gynergen and atropine in the treatment of scorpion poisoning in man. Barsoum, et al.[14] (1954) studied the pharmacological effects of the pure scorpion toxin on the dog and the uses of sympathicolytic and vagolytic drugs to counteract its ill-effects on the autonomic nervous system.

However, in spite of the fact that the literature on this subject is very voluminous, to the best of the author's knowledge, a

Year	Children Cases	Children Deaths	% of Deaths	Adult Cases	Adult Deaths	% of Deaths
1948	207	26	12.5 %	183	-	0 %
1949	199	22	11.0 %	218	1	0.4 %
1950	165	24	14.5 %	122	-	0 %
1951	207	31	14.9 %	215	-	0 %
1952	163	24	14.7 %	184	1	0.5 %

Table I. The annual percentage of deaths among children and adult cases of scorpion poisoning, treated in the casualty service, Manial University Hospital in the years 1948 to 1952.

detailed clinical study on the effect of scorpion poisoning in children is lacking to date. Such a study is, therefore, greatly indicated, especially as it is known that almost all fatalities from scorpion poisoning occur in children (Table I)[15]; and this is more so

in a country like Egypt, where scorpion poisoning in children is a very frequent casualty, ranking next to food and kerosene poisoning as can be seen from Table II[15].

	Number of Cases of		
	Food Poisoning	Petrol Poisoning	Scorpion Poisoning
1948	380	267	207
1949	667	448	199
1950	926	541	165
1951	882	502	207
1952	1164	518	163

Table II. The number of children cases treated for food, kerosene and scorpion poisoning in the casualty service, Manial University Hospital from 1948 to 1952.

CLINICAL STUDY

The material for this work consists of 450 cases of scorpion poisoning which were treated in Abbassia Children's Hospital over a period of four years (1953-1956). Of these, 250 cases were admitted to hospital and 200 cases were treated in the out-patient. The former group consisted of mild, moderate and severe cases, while the out-patient group were all mild cases.

Type of Patient: Almost all the cases were of the poor hospital class type, who live under rough hygienic conditions with much overcrowding and poor sanitation.

Seasonal Incidence: In the present series, it is found that the maximum incidence lies in the hot summer months, namely from May to September (Table III). Very few cases occur before or after this period.

	NUMBER OF CASES		
Jan.	—	July	112
Feb.	—	Aug.	91
Mar.	3	Sept.	57
Apr.	28	Oct.	9
May	58	Nov.	1
June	90	Dec.	1

Table III. The incidence of cases of scorpion poisoning studied in the different months of the year, over a four-year period.

It was also noticed that most of the cases reach the hospital during the night. These findings are explained by the scorpion's nocturnal habits, previously mentioned.

Age Incidence: Of the 450 cases, 10 per cent were children under 2 years of age, 46 per cent were from 2 to 5, and 44 per

cent were from 5 to 12. The relatively low incidence in children under 2 years may be related to the fact that during this age period, babies are usually under their mothers' more careful supervision.

SYMPTOMATOLOGY

Symptoms of poisoning usually appear within one quarter to two hours after the infliction of the sting. In some cases, symptoms of severe poisoning were fully developed within a quarter of an hour. This variation in the time of development of symptoms may depend on the rapidity with which the poison reaches the nervous system in sufficient concentration, which in turn depends on the site and vascularity of the area stung.

Clinically, the cases may present mild, moderate or severe symptoms, but, though we usually classify them as such, actually there is no sharp line of demarcation between one case and the other, and mild cases may gradually become moderate or even severe.

Mild cases are characterized by mild manifestations. These may only be local pain, or there may be some salivation as well, lacrimation or flushing of the face, with or without vomiting (once or twice) and little rise of temperature to 38°C.

Number Studied	Number and Percentage of Cases Showing							
	Local Pain only	Mild Temp.	Mild Lacrn.	Mild Salivn.	Mild Vomt.	Flushing of face	Pupillary Changes	Distension
100	40	37	37	27	27	18	12	5
	40 %	37 %	37%	27%	27%	18%	12%	5%

Table IV-A: Mild Cases.

In cases of moderate severity, salivation, lacrimation and flushing are usually more marked, vomiting is more frequent (3-5 times) and the temperature may rise to 39°C. Occasionally, there also may be slight nervous irritability, drowsiness, distension or diarrhea. Fluctuations in the blood pressure are usually mild.

Number Studied	Number and Percentage of Cases Showing									
	Vomt.	Hyperthermia	Lacrim.	Saliv.	Flushing of face	Mild Irrit.	Mild Drows.	Distension	Mild Fluct. in B. P.	Diarrhoea
75	57	52	33	30	24	18	12	12	9	2
	76%	70%	44%	40%	32%	24%	16%	16%	12%	3%

Table IV-B: Moderate Cases.

Severe cases, on the other hand, usually show a marked hyperpyrexia that may shoot up to 41.5°C. However, many arrive in a state of shock with sweating, subnormal temperature, thready pulse and a very low blood pressure. In the cases that survive this shock, reaction follows and the temperature gradually rises

and may reach hyperpyrexia. Vomiting is usually severe and persistent; in one case it numbered thirty-five times during the attack.

Number studied	Number				A Percentage of Cases Showing										
	Van.	Hyperthera.	Drows.	Irrit.	Lacrim.	Saliv.	Marked B.P. Changes	Schock & Imperceptible Pulse	Disten.	Flush.	Pupil. Changes	Convul.	Priapism	Diar.	Cyanosis & Respiratory Irritation
75	70	52	40	40	30	25	25	20	18	15	15	12	5 of 25 males	10	8
	93%	69%	64%	53%	40%	33%	33%	27%	24%	20%	20%	16%	14%	13%	11%

Table IV-C: Severe Cases.

It is not unusual for the vomited matter to become bloody. Frequently, there is marked nervous irritability, drowsiness, hallucination and possibly convulsions. In males, priapism was occasionally encountered in some severe cases suffering from irritability and convulsions.

Tables IV summarize the findings in the 250 cases studied in the in-patient.

As examples of the varied symptomatology, the following three cases are described:

Case 1 is a very severe one who died: G.A.A. is a male child, aged 2 years, admitted to hospital on July 27, 1956 at 7 P.M. stung two hours earlier by a scorpion in the left leg.

On admission, the pulse was 145, temperature 36.5°C., respiration 36 and B.P. $\frac{110}{70}$. There was excessive salivation and lacrimation, flushing of the face, marked irritability and severe distension. In hospital, his progress was as follows: (1) His temperature showed a gradual rise until it reached 40.8°C about ten hours after admission. This hyperpyrexia continued until the patient died four hours later; (2) The B.P. which was $\frac{110}{70}$ on admission, gradually dropped until it became unmeasurable four hours after admission, and continued as such for two hours, then showed some rise and seven hours later it was $\frac{70}{40}$; (3) Salivation and distension became more and more marked; (4) One hour after admission, vomiting and diarrhea began and gradually became more severe; (5) Irritability which was severe on admission continued for four hours, and then gradually diminished; (6) Priapism appeared two hours after admission; (7) Drowsiness started to appear three and one-half hours after admission, and gradually the patient passed into a state of coma; (8) The chest which was clear on admission, showed copious bronchial secretions

after eight hours and presented a picture of acute pulmonary edema; (9) Finally, the patient died in coma, hyperpyrexia and respiratory failure, fourteen hours after admission.

Treatment: (1) Antiscorpion serum (A.S.S.) combined with Dihydroergotamine and Bellafoline were given intramuscularly on admission, and four hours later; (2) For the hyperpyrexia, Novalgine drops were given and ice bags and iced sponges were applied; (3) For the irritability, bromides and luminal were administered; (4) For the chest condition, oxygen inhalation, Bellafoline and penicillin were given.

Case 2 is a severe case which survived the casualty: S.G.I. is a male patient, 11 years old, admitted to hospital on June 16, 1954, one hour after a scorpion sting in the left foot. On admission, he was in a state of severe shock, with a very rapid and thready pulse (140/min.), a subnormal temperature (35.5°C), rapid respiration (35/min.) and an unmeasurable B.P. He vomited three times before admission, and the vomited matter was bloody. In the reception room he was given A.S.S., and Bellafoline. In hospital, he became very irritable and drowsy and developed two attacks of convulsions. Vomiting was repeated four times more, and the vomited matter again was bloody. Two hours later, the temperature rose to 36.8°C and the B.P. to $\frac{100}{60}$. A.S.S. and Bellafoline were repeated, and Dihydroergotamine and luminal were also given. The patient subsequently showed a gradual and progressive improvement and he was discharged cured thirty-six hours after admission. It seems that the age of this patient (11 years) was an important factor in his relief.

Case 3 is another very severe case which also survived the casualty: N.H. is a female child, 5 years old. She was brought to hospital on September 6, 1956 at 10 P.M., half an hour after a scorpion sting in the right thigh. On admission, her temperature was 36.5°C, pulse 106, respiration 26 and B.P. $\frac{120}{80}$; her face was flushed and she was irritable and drowsy, and had already vomited five times before admission. In the casualty room she was given A.S.S., Regitine and Antrenyl. Two hours after admission her temperature reached 38.5°C, B.P. $\frac{130}{95}$, and she vomited three more times. The previous treatment was then repeated. During the second day the temperature fluctuated between 37°C and

39.7°C. Drowsiness and irritability persisted and she developed three convulsive fits at 6 P.M., 7 P.M. and 8 P.M. For the high fever ice bags and iced sponges were applied and for control of fits luminal was given intramuscularly. Later in the evening the blood pressure dropped to $\frac{70}{40}$ and the temperature reached 37°C. For the low blood pressure, antrenyl only was repeated. Next morning the blood pressure gradually returned to normal, the irritability and drowsiness gradually disappeared and the patient was discharged in very good condition twenty-four hours after admission.

PATHOLOGY

Unfortunately, the author could not obtain reliable post mortem data as the fatal cases were considered medicolegal and were transferred from hospital to the medicolegal department. However, Bert[6] (1885) experimenting on dogs, found that the most marked and constant feature at postmortem is a general congestion of the internal organs. He described also congestion and edema of the lungs. As regards the post mortem changes in the nervous system, Barros[9] (1939) in his experimental work on rabbits killed with the venom reported generalized hyperemia and vasodilatation of the brain, particularly evident in the medulla and pons. In nine out of twenty-two rabbits he noticed as well hematomata in the region of the pons and the medulla resulting from rupture of the basilar artery. Microscopically, he found hyperemia of the brain and marked capillary dilatation, with changes in the vegetative centres, consisting of cellular swelling, liquefaction and chromatolysis. Silver stain showed pronounced hyperchromasia and swelling of the intracellular neurofibrils of the pons and medulla. Since the cells of the vegetative centres were specifically damaged, Barros, expressed the belief that the venom has a selective effect on these centres and he considered that the symptoms of scorpion poisoning support this concept.

PROGNOSIS

Undoubtedly, the severity of the condition will depend primarily on the type and the amount of poison that could be poured by the scorpion into its victim. However, in the present study, the following points were found of importance when judging the prognosis, namely:

(1) *The age of the patient.* It was found that the younger the

patient, the more severe the symptoms and the worse is the prognosis (Table V). This could be explained by the fact that the amount of venom per kilogram body weight of the victim is greater in younger children than in older ones.

	Total Number	Number of Deaths	% of Deaths
Cases below 2 years	30	7	23.3 %
Cases between 2 & 5 years	115	16	13.9 %
Cases between 5 & 12 years	105	5	4.0 %

Table V. The relation of the age of the patient to the prognosis.

(2) *Relation of time to the prognosis.* The following remarks could be obtained from the study of the present series. (a) The longer the period that elapses from time of sting to admission, the more severe would be the symptoms (Table VI). This could be attributed to the fact that the longer time before treatment gives opportunity for more venom to be absorbed and to act on the different systems and vital centres.

	The Period from Time of Sting till Admission		
	½ an hour or less	½ to ¾ hour	1-1½ hrs. 2 hrs. or more
100 Mild Cases	14 = 14 %	32 = 32 %	34 = 34 % 20 = 20 %
75 Moderate Cases	6 = 8 %	21 = 28 %	30 = 40 % 18 = 24 %
75 Severe Cases	3 = 4 %	15 = 20 %	32 = 42 % 25 = 33.3%

Table VI. The relation of the period that elapse from time of sting to admission and to the prognosis.

(b) If 6-8 hours elapse with or without administration of treatment, and no severe symptoms appeared, then usually the prognosis is good.

(c) In severe cases, if the patient survives the first forty-eight hours, then in all probability he will escape death. Recovery, when it occurs, is always complete, leaving no residual effects.

(3) *Certain symptoms were noticed to be of bad prognostic significance, namely:*

(a) Marked and persistent hyperpyrexia. (b) Repeated convulsions. (c) Marked irritability and drowsiness. (d) Priapism. (e) Repeated vomiting, especially if bloody. (f) Severe drop in blood pressure.

(4) *Site of sting.* It was found that stings located nearer to the central nervous system as in the scalp, lumbar region, shoulder or

thigh, usually gave earlier and more severe symptoms than stings situated more peripherally as in the fingers, toes, hands and feet. This may be due to the fact that the poison in the former cases is rapidly absorbed due to increased vascularity of these areas or that some of the venom in part ascends directly to the central nervous system along the perineural lymphatics.

TREATMENT

On arrival, all cases were given the antiscorpion serum to neutralize the circulating venom. It is senseless to give up the time honored therapy with the serum and to depend wholly on drugs. Such trials would mean no more than risking the lives of our patients pointlessly. Serum treatment was usually sufficient in mild cases, but in moderate and severe ones, other drugs were added. Mild cases, however, should be kept for a sufficiently long time under observation, so that should more severe symptoms develop later, the serum may be repeated and other measures may be taken. Two of the mild cases that refused to wait in hospital after taking the serum injections returned to the hospital six and eight hours later in a moribund condition and could not be saved.

For moderate and severe cases other drugs were given together with the serum. The basis for this drug therapy depends on the fact that the venom acts as a stimulant to both the autonomic[11] and the central[15] nervous systems. Consequently, drugs used should act as antidotes physiologically antagonistic to the action of the venom on these systems. For combating the hyperpyrexia caused by the foreign proteins of the scorpion poison entering the blood, Novalgine was given and ice bags and iced sponges were applied. Either Dihydroergotamine (D.) (0.015 mg./kg.) or Regitine (R.) (0.15 mg./kg.) were given as sympathetic paralysants, while Bellafoline (B.) (0.008 mg./kg.) or Antrenyl (A.) (0.015 mg./kg.) were given as parasympathetic paralysants. To secure a rapid effect, these drugs were given by the intramuscular route. For control of central excitation which was usually evidenced by marked irritability and convulsions, bromides and luminal were usually given. Morphia was avoided and should strongly be prohibited for fear of respiratory depression as it is known that scorpion poison, in severe and moribund cases, acts as a central depressant to respiration. Oxygen inhalation when needed was given. When necessary, serum with one or more of the drugs previously given were repeated at four hour intervals. The critical period in which it was necessary, in some instances, to repeat administration

of the drugs usually did not exceed forty-eight hours from the time of the sting.

Early in this study, the routine treatment was to give sympathetic and parasympathetic paralysants in conjunction with the serum to all moderate and severe cases. This was found to give good results only in cases showing symptoms suggesting stimulation of both sympathetic and parasympathetic systems. On the other hand, at a stage where symptoms of parasympathetic stimulation prevailed and were most serious, as when there was marked drop in blood pressure, with imperceptible pulse, severe vomiting and sweating and excessive bronchial secretions, this treatment either failed, or made the condition worse. When, however, parasympathetic paralysants only were given at such stages, many lives could be saved.

Results of Treatment: 1. All mild and moderate cases were cured; 2. Of seventy-five severe cases treated in the in-patient, twenty-five died. This makes a mortality of 33.3 per cent for the severe cases, 10 per cent for the 250 cases treated in the in-patient and about 5½ per cent for the whole series of 450 cases treated in the in- and out-patients. This 5½ per cent mortality is rather good when compared with 11 per cent to 14.9 per cent mortality for the children cases treated in the casualty service at Manial University Hospitals between 1948 and 1952, (Table I). In the latter cases, the routine treatment was serum combined with Gynergen only; 3. When the effect of treatment with serum combined with Regitine and Antrenyl (S + R + A) is compared with the effect of treatment with serum combined with Dihydroergotamine and Bellafoline (S + D + B), the following observations were made.

(I) Both lines of treatment are equally successful in saving all cases of moderate severity. (Table VII).

	Moderate Cases			Severe Cases		
	Number of Cases	Number of Deaths	% of Deaths	Number of Cases	Number of Deaths	% of Deaths
S + R + A	30	0	0 %	30	9	30%
S + D + B	40	0	0 %	42	14	33.3%

Table VII. Comparative study of the effects of combining S + R + A and combining S + D + B in treatment of moderate and severe cases of scorpion poisoning.

(II) In severe cases, however, treatment with combined (S + R + A) gave somewhat better results than treatment with

combined (S+ D + B). The mortality was 30 per cent in the former group and 33.3 per cent in the latter (Table VII). However, the number of cases treated by either combination is rather insufficient to allow for a definite conclusion in this respect, and at present, further study on this point is still being carried out.

SUMMARY AND CONCLUSIONS

(1). 450 cases of scorpion poisoning among Egyptian children were clinically studied.

(2). The age and seasonal incidence are registered.

(3). The symptomatology is given in detail, together with tables summarizing the symptoms noticed in mild, moderate and severe cases in their order of frequency. Three case reports are recorded as examples.

(4). The points that are important in judging the prognosis are discussed.

(5). The main lines recommended in the treatment are stated, together with some important remarks.

(6). A preliminary comparative study on the effect of combining serum with Regitine and Antrenyl and of combining serum with Dihydroergotamine and Bellafoline in treatment of moderate and severe cases is also given, and the results obtained are noted and discussed. Further work on this subject is still being done.

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PHYSICAL FITNESS OF SCHOOL CHIDREN IN THE UNITED STATES

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In the years 1925 and 1926, the author, in cooperation with the New York City Department of Health and the Board of Education conducted a physical fitness demonstration in several elementary schools. The program was based on the premise that the teaching of proper health habits and the overcoming of improper health habits that have led to physical unfitness is as much a concern of the school as is the teaching of proper habits of thinking through mental education. Not much interest was shown in this subject through the years following. It was not until twenty-five years later, in 1950, that the Health Council of Greater New York based on a survey by the School Lunch Committee stated as one of its recommendations: "Much can be done to improve the program by developing a better understanding of nutritional needs and goals of the program on the part of principals and teachers. An integrated education plan in this direction should be instituted, parent participation should be encouraged and a greater effort made to utilize the program for improving the children's food habits." These conclusions, expressed by qualified personnel working in this field, support the validity of the basic concept of the responsibility of the schools as expressed by the writer twenty-five years ago.

Recently, the President of the United States alarmed by reports of observers expressed his deep concern regarding the extent of physical unfitness among our children. It has been estimated that twenty-five to forty per cent of school age children fall into this category. In these days of international tensions, when an arduous and devastating war is always a possibility, our thoughts are directed to the question of whether our children will grow into young adults who will be able to bear the physical strain of military as well as civilian life. This is not the only reason for the quest for physical fitness. The physically unfit among our

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younger generation have been shown to be about six or seven times more susceptible to upper respiratory infections and at least three times more susceptible to tuberculosis. The child who attains physical fitness is likely to acquire and maintain greater mental alertness and will be better equipped to enter his chosen sphere of life.

Any proposed program to correct this situation will succeed only if it recognizes the responsibility of the school toward those children who have fallen by the wayside in physical fitness. They must not be subjected to any vigorous physical exercise as may be required of the children of normal growth and development. They require health instruction of a different nature. A program suited to their needs and intended to bring them up to a normal state of physical fitness will be presented in subsequent paragraphs. That such a program can be carried out successfully in schools, without creating any special classes and any additional costs, was demonstrated by the writer in the above-mentioned project in Queens County, New York City schools.

It may be asked what is meant by physical fitness and unfitness in school children. It is not necessary to ask ourselves—fitness for what? The child has but one occupation—the acquisition of knowledge and suitable habits that will lead to normal mental and physical well-being. If we were to use another word for physical fitness, it would be the word *health*. It means more than the absence of disease. We do not have any acceptable laboratory tests that can give an accurate diagnosis of physical unfitness in a child. However, the physically fit as well as the physically unfit can be readily recognized. The latter is considerably underweight for his height; he is apt to hold his mouth open due to naso-pharyngeal obstruction; he stands with his head set forward, hair dry and dull; the shoulder blades stand out prominently; the abdomen protrudes; the knees are slightly bent, and the feet are flat and pronated. The physically fit child stands erect; his eyes are bright; his hair is glossy; he walks with a springy step; his appearance is vigorous and alert and he is of normal weight for his height.

The causes of physical unfitness in school children are as follows: Physical defects; Lack of home control; Over-fatigue; Poor food and food habits; Poor health habits.

The most frequent physical defects responsible for impairment in growth and development are chronically diseased and hypertrophied tonsils and adenoids. Experience has shown that failure

to remove these defects in children may make difficult the attainment of physical fitness. Furthermore, their presence may cause severe complications in childhood infectious diseases. Continued mouth breathing also may be responsible for deformities of mouth and pharynx. Other defects include acute and chronic diseases, dental caries, and postural defects. Failure of discipline and self control may lead a child into acquiring faulty food and health habits and contributes to his failure to attain normal development. Over-fatigue does not refer to the normal fatigue after exercise, but rather to the persistent over-activity which keeps the child in a chronic state of exhaustion.

An adequate school physical fitness program is divided into two parts. The first concerns itself with the care of the physically unfit, that is, to bring them up to the normal level. In this phase of the work, the doctor takes a leading part. He supervises the selection of children for this group. He does the physical examinations and directs the correction of physical defects. He prescribes a daily program for the child that will lead to the acquisition of proper food and health habits. Where progress has been unsatisfactory in any individual case, he will do a re-examination to determine if some physical defect or other factor has been overlooked. Where laboratory tests and closer observation and study are required, he may recommend hospital admission. While the doctor prescribes the rules of healthy living, inculcating them into the daily life of the child is the function of those entrusted with the child's education, namely, the school. A program such as this should be pedagogically as well as medically sound. A child will not acquire desired health habits by didactic teaching. He learns by actual performance. The repetition of an act will form a habit. Thus it is necessary to put the child on a definite daily program. Health habits attained and maintained during the period of growth are likely to continue throughout life. Such a program should begin in the lowest grade when the child also begins his mental education.

The following are suggested procedures for the organization and conduct of a school program for the care of the physically unfit children.

1. The children in the entire school are examined by the school physician.

2. The weight and height of the children are recorded. Those who are more than 7 per cent underweight for their height are

eligible for admission to the group for special attention. This is the simplest way of picking the physically unfit, particularly when dealing with large groups. These children will show the above mentioned symptoms and signs of physical unfitness.

3. The children, admitted to this underweight group, require a more detailed physical examination. This can be done by the school physician or by the family doctor using a special form which should include a statement of the child's food and health habits, an outline of his activities during the non-school hours, as well as a personality examination.

4. A physical fitness class is organized and should meet once a week for about three-quarters of an hour. Each child will leave his regular class for this session. The parent or guardian is expected to attend. The children should be weighed each week, and their weight recorded on large individual charts hung where they can be readily seen. The diet books will be checked, problems raised by the parents will be discussed, and a "pep" talk given by the teacher in charge of the class session.

5. A daily program of food and rest periods is outlined, a diet book is given to each child, where the daily intake, activities, and rest periods, are recorded for two average days of the week. The underweight child will require between two to three thousand calories per day. The requirements of a daily program and general suggestions may be incorporated in a form, mimeographed and attached inside the cover of the diet note books.

CHILD'S DAILY PROGRAM

Breakfast

Fruit juice; Cooked cereal; Egg, boiled or scrambled with milk or cream or fried in butter; Bread (preferably whole wheat or enriched white) and butter; milk

Mid-morning lunch

At home or at school—to be followed by rest:
Two graham crackers; One bottle or glass of milk

Lunch

At noon, the meal to include among other things, a vegetable in addition to potato

Mid-afternoon lunch

At home or at school, to be followed by rest

Dinner

To include among other things, bread and butter; Milk

GENERAL SUGGESTIONS

Three glasses of milk each day; no tea nor coffee.

No sweets between meals; however, candy may be eaten right after dinner.

Eat slowly, chew food well. Do not wash food down with liquids.

Eat some fruit and vegetables daily.

During rest periods, lie flat on back or stomach, open windows, no reading or studying during rest periods. Take long rests Saturdays, Sundays and holidays.

Unless permission is given, do not carry on any activities beside school work.

Go to bed at 8 o'clock every night, windows open.

The more you eat and rest the more you will gain.

During the weekly class sessions, the teacher or a dietician employed by the school, or a voluntary assistant, may offer advice to the parents as to foods and their preparation. Where the physical examination discloses the presence of a specific avitaminosis, the child should be referred for treatment to the family doctor or hospital clinic. The mid-morning or mid-afternoon lunch is made a definite requirement. As already stated, gymnastics are contraindicated for the children in this group. They need rest periods instead. These may be taken when the other children have their regular physical training. Where space for this purpose cannot be made available, the rest periods at home are essential.

When a child reaches the average weight for his height, it may be advisable to continue him in the group until he has reached his optimum weight. A veritable transformation will then have taken place. Not only will improvement be noted in his physical state, but also in his mental capacity. In a demonstration program, by the writer of only twelve week's duration, repeaters (those left back in school) were reduced from twenty-three per cent to fifteen per cent which was the figure for the entire school. There will also be noted an improvement in the behavior pattern of the children who have attained physical fitness as a result of this program. This has been accomplished by the self discipline practiced by the children to obtain their goal, and which may well become a permanent facet in their character. The graduates of the group join the rest of the school in the regular physical training. They

will, of course, undergo the regular annual or semi-annual school physical examination and will thus be under observation for their entire school career. A program, such as described, should begin with a group of twenty-five or thirty children to be obtained from the lowest grades.

The second part of the schools physical training program concerns itself with the children of normal growth and development and with those who are less than 7 per cent underweight. Here the doctor steps aside and the physical training instructor takes charge. His function is to prescribe and direct physical exercises that will aid in the growth and development of the child, and will tend to increase and maintain his physical capacity. The exercises should be of such a nature as to fit the needs of all the children. The training of the school population must not be subordinated to the training of the school teams. The form of exercise that can be engaged in by practically all pupils in the group under consideration here, not merely while still at school but also in later life, is calesthenics. Performing this type of exercise in unison in ever enlarging groups will engender pride in the attainment of proficiency. It will also broaden the base for selection of candidates for the school teams.

Credit marks given for effort as well as for accomplishment should be considered of equal importance with marks for mental effort and achievement. There will, of course, be a small percentage of pupils who have physical defects that cannot be corrected for whom special consideration will be shown. In general, physical fitness is attainable. Where a suitable program exists, those students who through lack of interest fail in this goal, may not be proper material for higher learning or even for the better type of employment in the business world.

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USE OF GLUCOSAMINE-POTENTIATED TETRACYCLINE* IN THE TREATMENT OF UPPER RESPIRATORY INFECTIONS IN CHILDREN

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Considerable interest and research efforts continue in the direction of broadening the spectra of antibiotic activity both in the development of new drugs, and with new combinations of established antibiotics. However, within the past few years a new research trend appears to have provided what may well be termed a 'second dimension' in antibiotic effectiveness—the increased *height* of serum antibiotic levels with absorption-enhancing products.

The first effects of such research resulted in the development of several agents which, upon initial study, appeared to enhance absorption of tetracycline.[1-3] However, further examination revealed their action to be the result of the removal of certain excipients employed in commercial encapsulation which depress absorption of the antibiotic.[2,4] Thus, in the absence of such depressants re-evaluation of the action of available absorption-enhacing agents appears to have pointed up their limited effectiveness.[5]

Recently a new compound, glucosamine, has been under investigation as an absorption-enhancing agent for antibiotics. With the elimination of any depressant excipients, the combination of glucosamine with tetracycline or oxytetracycline was found to provide higher antibiotic serum concentrations than either antibiotic alone.[6] Subsequently in a 4-way crossover study, it was reported that the oral administration of glucosamine with tetracycline effected antimicrobial levels superior to those obtained from all enhancement formulas currently available (tetracycline phospate complex, tetracycline plus citric acid, and tetracycline plus sodium hexametaphosphate).[7]

Most recently, glucosamine with tetracycline (Cosa-Tetracyn) has proved to be clinically effective in gynecologic infections,[8] upper respiratory infections,[9] and dermatologic infections or secondarily infected skin diseases.[10] In the latter study it was concluded that based upon past experience the administration of tetracycline (2 gm. daily) and glucosamine was clinically more

* Cosa-Tetracyn (brand of glucosamine-potentiated tetracycline) was supplied for this study by Pfizer Laboratories, Brooklyn, N. Y.

effective than the antibiotic alone.[10] This effect would seem to be the logical result of the higher antibiotic serum concentrations as reported for glucosamine-potentiated tetracycline.[6]

Chemically and physiologically, glucosamine appears to have established a new class of absorption-enhancing compounds. It is a biologically important aminosugar which occurs naturally in the human body, and is present in the serum in approximately the same concentration as glucose.[11,12] For purposes of clinical evaluation, glucosamine appears to be nontoxic. It is an extremely safe compound apparently even in administration of massive doses.[13]

While clinical studies on adult patients generally precede any pediatric studies with a new product, such results are not necessarily duplicated in children or infants by a simple reduction in dosage. Initial treatment of upper respiratory infections in children is often difficult because of the frequency of such infections, and because accurate etiologic diagnosis is not always available, hence the antibiotic selected may not be specific for the organism. The complexity of choice has also been compounded by the advent of staphylococcic infections, in children as well as adults, which are resistant to many of the more commonly used agents.

The selection of Cosa-Tetracyn for the treatment of upper respiratory bacterial infections in infants and children was based upon several considerations. Since no broad-spectrum antibiotic is available for initial treatment of *all* such infections in children and infants, obviously the broad-spectrum drug which provides the most immediate and efficient antimicrobial attack is the therapy of choice. The reported superiority of glucosamine-potentiated tetracycline over other preparations, its rapid achievement of higher antibiotic serum concentrations over tetracycline alone (averaging 105 per cent at the 2-hour interval), as well as the possibility of its *clinical* superiority over tetracycline, were important factors influencing initiation of the study described below.

METHOD

Fifty patients were treated for various upper respiratory infections or complications thereof. Forty-nine patients, ages 6 months to 14 years, and one patient age 20 years received Cosa-Tetracyn for oral suspension, reconstitituted to 125 mg. of glucosamine-potentiated tetracycline syrup per teaspoonful (5 cc.). In all cases, the drug was administrated at 4-hour intervals. The majority of patients (39) received one teaspoonful of the syrup per dose. However, five patients ages 6 to 16 months received

Table I

SENSITIVITY AND RESISTANCE TESTS

Diagnosis (50 Patients)	Pathogenic Organisms										Antibiotics			Results of Treatment with Glucosamine-Potentiated Tetracycline
	Streptococcus	Beta-hemolytic streptococcus	Diplococcus	D. pneumoniae	N. pyogenes	var. albus	H. saturhalis	H. influenzae	Pseudomonas	P. aeruginosa	Penicillin	Tetracycline	Chloramphenicol	
Pharyngitis			X			X					R	Sl	V	Not cured
"		X	X		X						M	M	M	Not determined*
"					X						S	S	S	Cured
"			X	X		X					R	Sl	S	"
"			X		X						S	S	S	"
"			X	X		X					Sl	Sl	Sl	"
"			X	X		X					Sl	M	S	"
Pharyngitis, otitis media			X	X		X					S	S	S	"
" " "			X	X		X					Sl	S	S	"
" " "		X		X		X					M	S	S	"
" " "						X					Sl	V	V	"
Pharyngitis, bronchitis			X		X	X					S	S	S	"
" "			X	X			X				S	S	S	"
" "			X					X			Sl	S	S	"
" "			X			X					S	S	S	"
Pharyngitis, stomatitis			X	X		X					M	M	S	"
Pharyngitis, cervical adenitis					X	X					S	S	S	"
Pharyngitis, furunculosis			X			X			X		S	S	S	Not cured
Pharyngitis, multiple staphylococcic abscesses						X					R	M	S	Cured
Tonsillitis			X		X	X					R	M	S	"
"			X	X		X					R	Sl	Sl	"
"			X		X					X	S	S	S	"
Tonsillitis			X	X							S	S	S	Cured
"				X		X					R	M	S	"
"			X			X					S	S	S	Not cured
"			X	X		X					S	M	M	Cured
Tonsillitis, otitis media				X		X					R	R	S	Not determined**
" " "		X		X		X					S	M	M	Cured
" " "			X	X		X					S	S	S	"
Bronchitis						X					Sl	Sl	Sl	"
"			X			X					Sl	Sl	S	Not cured
"				X		X					S	M	S	Cured
"						X					M	M	S	"
"			X	X			X				R	S	S	"
"			X		X						S	M	S	"
"			X		X						S	M	S	"
Bronchitis, otitis media			X	X		and gram-negative cocci					Sl	S	S	Not cured
Otitis media		X		X		X					M	M	S	Cured
" "			X	X							M	S	S	"
" "			X	X		X					Sl	V	S	Not cured
Pneumonitis										X	R	M	Sl	Cured
"			X	X							S	S	S	"
"		X			X	-					Sl	Sl	S	Not cured
"			X	X		-					V	S	S	Not determined**
Croup			X	-		-					S	Sl	S	Cured
"			X				X	X			Sl	R	S	Not cured
"		X		X		X					R	M	M	Cured
"			X	X			X				Sl	S	S	"
"		X		X		X					M	V	M	"
Croup, pharyngitis			X			X					Sl	S	S	Not cured

V - Very sensitive
S - Sensitive
M - Moderately sensitive
Sl - Slightly sensitive
R - Resistant

* Patient developed measles
** Patient cured with Glucosamine-Potentiated Tetracycline plus penicillin

one-half teaspoonful, 4 patients ages 3½ to 14 years were given two teaspoonfuls, and 2 patients ages 16 months and two years received one teaspoonful in addition to 300,000 units of penicillin.

Forty-five of the fifty patients received the drug from one to three days. The remaining number were treated for the maximum period of four days.

Sensitivity tests were done by means of the medicated disc method employing penicillin, tetracycline and chloramphenicol. In all cases cultures of clinical specimens from the nose and throat were used.

RESULTS

Of the fifty patients seen in private practice who received Cosa-Tetracyn syrup for upper respiratory infections, or coincident complications such as otitis media, thirty-eight were cured and nine failed to respond to therapy within a predetermined period of four days. Results in the remaining three patients were labeled "not determined" though two were cured and a third became afebrile within 24 hours. The individual effect in two of these cases, though cured, could not be determined since 300,000 units of penicillin had also been administered to each. With remission of fever in the third patient, signs and symptoms of measles were manifested and therapy was discontinued.

Treatment resulted in an even higher effectiveness in patients suffering from mixed infections which specifically included staphylococci resistant to penicillin *in vitro*. Nine of ten such cases were cured following the administration of the drug, a recovery rate higher than that of the entire group reported here.

Another finding of interest was that two other cases with infecting bacteria exhibiting *in vitro* resistance to tetracycline were cured with administration of Cosa-Tetracyn. It can only be concluded that here, again, there is a failure of correlation between laboratory susceptibility tests and clinical therapeutic response. The serious consequences which could result from failure to administer a potentially curative antibiotic because of a negative sensitivity report are only too clear. While only two cases of this type were encountered here, the results are comparable to findings reported by Stone, et al.[8] Additional clinical evidence obviously is required to evaluate this effect, but the possibility of its medical significance as related to higher antimicrobial serum levels attained more rapidly, should stimulate further investigation.

Response to treatment with Cosa-Tetracyn was good in all

cases. The period of treatment ranged from one to four days, the average time required for cure being approximately 2.5 days.

The preparation was extremely well-tolerated; side effects were mild and transitory. The infrequent occurrence of loose stools in eleven patients did not necessitate interruption of therapy.

SUMMARY

Cosa-Tetracyn is a new form of tetracycline, strongly potentiated in absorption capability by the addition of the aminosugar D-glucosamine. Fifty children, seen in private practice, with upper respiratory infections were treated with this drug; of these, thirty-eight were cured, nine failed to respond to therapy within the predetermined period of four days, and therapeutic effect could not be determined in three cases.

Ten of the patients in this series had staphylococcic infections resistant to penicillin *in vitro*. Nine of these were cured with the glucosamine-potentiated tetracycline. The clinical results obtained with Cosa-Tetracyn give support to the laboratory evidence of heightened absorption and increased tetracycline blood levels.

Glucosamine-potentiated tetracycline was extremely well tolerated. Side effects in this series were limited to infrequent loose stools. The need to cease or interrupt therapy was not indicated in any instance.

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AN EVALUATION OF URIC ACID AS AN ETIOLOGICAL FACTOR IN SOME OF THE OBSCURE PATHOLOGIES

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Although some of the pathologies involving hyperuricemia are the oldest known to medical science, comparatively little has been uncovered concerning the pathogenesis of these diseases; nor has sufficient emphasis been placed on the unique position which uric acid holds in the metabolism of proteins, or upon the role which it plays in the development of some of the obscure disorders of the body.

In evaluating the etiological position of uric acid in a broad range of pathologies, from the rheumatoid-arthritis group to that of the neuropathological, the following aspects of uric acid study must be considered: (1) the evolutionary aspects of uric acid metabolism, (2) the hereditary factors of uric acid metabolism, (3) the physico-chemical qualities of uric acid, (4) the disordering effects of uric acid in the oxidative-reductive cell processes, (5) the effect of uric acid accumulation on phosphate metabolism, (6) early symptoms of uric acid toxicity, (7) the rheumatoid disorders, (8) ordinary gout, (9) irregular gout, (10) neuropathological involvement, (11) the comparative advantages and disadvantages of uricosuric medicaments, (12) dietary comments.

In evolutionary studies involving physiological chemistry in different species of mammals, man is unique in that he eliminates 90 per cent of his purine-allantoin nitrogen in the form of uric acid. This quantity is eleven times that of the monkey which is biologically his closest relative, but this ratio is known to vary considerably within a species. The variations in uric acid excretion are attributed to a purely evolutionary facet in mammalian development and are related to the comparative water retentive qualities of uric acid as compared with that of urea, the waste product of more highly developed species.

This evolutionary aspect of protein metabolism evidently extends to a hereditary continuance of tendencies towards excessive uric acid production, for hyperuricemia is found in 25 per cent of blood relatives of those affected, with women being less affected. These evolutionary and hereditary aspects of uric acid production in man must, however, always be examined in the light of the quan-

tity of purine ingestion. Since many of the hyperuricemia disorders are familial, the likelihood exists that dietary similarities may be accentuating the hereditary tendencies.

Pure uric acid is a white, crystalline, tasteless and odorless substance, requiring 15,000 parts of cold water for its solution. It is a weak, dibasic acid, forming normal and acid salts of limited solubility. Normal sodium urate is soluble in 62 parts of water, the acid salt in 1,100 parts of water. When oxidized, uric acid produces parabanic acid, barbituric acid or related products of great toxicity. It is these physico-chemical characteristics of solubility, salt formation and oxidative products that link uric acid with the extreme chemical disturbances of the body which produce those pathologies which have been so difficult to trace.

In man, uric acid may be divided into two varieties, endogenous and exogenous. The endogenous uric acid represents that formed in the body by synthesis and by the breakdown of nuclear tissue. It comprises about .4 gm. per day, varying little in different persons. It is, most likely, the oxidative product of hypoxanthine which is constantly forming in muscle and other tissues. The exogenous uric acid is that formed by the oxidation of purines taken in as part of the food, chiefly meat. All meat contains varying amounts of nucleic acid which, in turn, contains about 20 per cent of the purines, *adenine* and *guanine*. Glandular meats, such as the liver and sweetbreads, are particularly rich in the purines, but adenine and guanine are also found, to some degree, in poultry and in the leguminous vegetables.

Because man lacks a specific enzyme, uricase, which converts uric acid into allantoin, it is functional for him, as contrasted with other mammals, to excrete ingested purines almost entirely as uric acid. However, since 90 per cent of the uric acid that enters the glomerular filtrate is reabsorbed in the renal tubule, man's efficiency in uric acid elimination is limited, his normal clearance being about 7 per cent to 16 per cent.

In the blood stream, under normal conditions of production and removal, the body contains a soluble or miscible uric acid pool of about 1.2 gm. of which about 700 mg. to 850 mg. are turned over daily, representing normal formation and disposal of uric acid. The normal uric acid content of whole blood is 2 mg. to 4 mg. per 100 cc. and is usually little affected by ingestion of purine rich foods. The uric acid content of urine, however, normally varies directly with purine intake and is also affected by the protein and caloric content of the diet.

When disturbances occur in the uric acid metabolism, the uric acid output in the urine is lowered and, as the individual ingests more purines, there results an accumulation of uric acid. This storage first takes place in the blood but, owing to the characteristic of low solubility of the uric acid and its salts, only a limited amount can be controlled by the buffering quality of the plasma. The excess of uric acid may remain, within the limits of its solubility, in the intercellular fluids or in the fluid protoplasm, or it may crystallize in the various parts of the body as acid sodium urate, resulting in irritation and inflammation. The acid sodium urate produces pathologies characteristic of the area in which it forms, for example, in the kidney, lithasis results; in the bursae, bursitis; in the cartilage and joints, gout; along the sciatic nerve, sciatica; in the synovial membranes and sclerae, rheumatoid arthritic inflammation.

This mobilization of excess uric acid in the form of sodium salt is a regular manifestation of uric acid accumulation, readily recognizable by the diagnostician. It is less easy, however, to distinguish that type of irregular or indeterminate form of uric acid accumulation when the excess is suddenly precipitated into the tissues as pure uric acid. This phenomenon may be excited by exposure to cold, fatigue, overwork either physical or mental, and is usually precipitated, most violently, in situations where the body is exposed to a continuous term of extreme physical rigor accompanied by excessive perspiration.

It is likely that, under these extremities of exertion, in addition to the reduction of body fluids affecting the solubility of uric acid, there is a further adverse effect made upon tissue solution of uric acid by the excessive production of sarcolactic acid. This type of irregular gout may affect persons who observe the strictest temperance in living and whose only excesses are either physical or intellectual overwork. Previous history has indicated that most cases of this uric acid self-intoxication occur between the ages of 20 and 50. However, since there is a definite evolutionary and hereditary pattern in uric acid accumulation, the researcher cannot discount the possibility that a broader range of years and pathologies may be uncovered by a closer examination of uric acid precipitation phenomena.

Before proceeding to an examination of these pathologies, it is important to detail the following aspects of uric acid accumulation.

1. In blood examination for uric acid, hyperuricemia is ap-

parently not the cause of the acute symptoms of the usual pathologies produced by this toxicity.

2. There is no constant quantitative correlation between the clinical response and the plasma urate lowering effects of the uricosuric preparations.

3. Administration of uric acid orally or intravenously does not precipitate an attack.

4. The maximum apparent solubility of uric acid in whole blood is 6.16 mg. per 100 cc.

5. Despite the fact that the maximum normal of uric acid in whole blood is 4 mg. per 100 cc., an examination revealing an abnormal quantity would merely indicate that the patient is gouty, rheumatoid, etc.

6. Relatively large quantities of uric acid are found in infants. This amount gradually diminishes as the child develops. Whether this greater tolerance of uric acid is true, or merely reflects the fact that throughout childhood it is unusual to expose the body tissues to the stresses and strains that cause uric acid precipitation, is open to examination. Certain childhood conditions with rheumatoid implications will be examined for their possible uric acid etiology later in this study.

7. It is equally apparent that in the female the tolerance for uric acid may not be true, for in addition to the fact that they are less often exposed to the tissue rigors of the male, they also enjoy a natural estrogenic barrier against the usual disorders that occur under hyperuricemic conditions. This measure of immunity gradually diminishes with age, and all of the pathologies with uric acid significance are found in the older woman. This is particularly true of those in laborious employment, such as charwomen, or housewives under great physical and nervous stress.

8. Of great significance to this study is the dietary development in our modern society. According to the Food & Nutrition Board of the National Research Council, the recommended daily dietary protein allowance for normal, vigorous men between the ages of 25 and 65, weighing 143 pounds, and 5 feet 7 inches in height, would be approximately 2 ounces. There is comparatively slight variation in a lesser direction for young children and women; in a greater direction for older children, pregnant or lactating women. In light of the greatly increased use of protein in our diet today, the danger of tissue uric acid accumulation by overproteinization is apparent.

9. Overvitaminization is also a contributing factor to excessive uric acid formation, affecting the endogenic production. Liver extract, vitamin B_{12} and, most likely, excessive use of vitamin C and B_1 increase tissue uric acid. This overvitaminization may take place through the use of concentrated synthetics or vitamin-rich juices and glandular meats. This is particularly true of the water soluble vitamins whose cold season use has been expanded beyond the body's requirements.

Hyperuricemia in its manifestations beyond the rheumatoid and gout forms develops into non-determinate, pathological forms which are hyperkinetic and neuropathological. One of the essential causes of change in the environment of the neurones is an abnormal condition of the blood and lymph. This ecological change for the neurones can be produced by the excess of certain normal constituents of the blood, such as the nitrogenous wastes. If oxidation of this material is incomplete or these substances accumulate in the blood, uremia supervenes with symptoms of polyneuritis, coma, or convulsions. This type of toxicity can also be produced by a number of perverted or incomplete organic functions, among which is an excess production of uric acid. All of these act in the cerebro-spinal fluid in which the neurones are bathed. This autointoxication affects the nervous system. It usually establishes a vicious circle which is constantly enlarging with increasing neuropathological gravity, but is not always reflected by greatly increased uric acid in the cerebro-spinal fluid. As in the earlier mentioned disorders, the uric acid may have been precipitated directly into the nerve tissue cells.

Among the general disorders that produce a neuritis of the type described, rheumatism and gout have always had a prominent position. It has also been recognized that Bell's palsy can be attributed to the inflammatory swelling and compression of the facial nerve following exposure to a cold draught in a person with a rheumatic diathesis. Similarly, sciatica is produced in the gouty or rheumatic and follows exposure to cold and wet. It is important to note here that multiple neuritis and muscular dystrophies not involving any discoverable change in the nervous system follow the hereditary patterns of uric acid accumulation. These latter pathologies, together with those previously mentioned, reveal congenital relationships, family patterns, transmission of hereditary tendencies by women who are rarely themselves subjects. It may affect children of both sexes but the majority of cases are male.

After careful observation, it is the opinion of this worker that, as the vicious circle of neuropathological toxicity expands, it produces all of the symptoms of paralysis agitans (Parkinson's disease). It is also of interest to note that the discomfort of paralysis agitans is best ameliorated by the same treatment as that of the gouty and rheumatic, that is, rest in bed, attention to the respiratory functions, nutrition, and excretion.

There also appears to be a parallel to uric acid accumulation in the history of rheumatic fever with heredity commonly supposed to be a predisposing cause. Here, too, the elements of stress and strain, exposure to wet and cold are revealed by the fact that rheumatic fever never occurs before the age of two, and that studies in England show that it occurs during the wet and cold seasons from October to March.

As the rheumatic fever of childhood develops into its chronic forms, the hyperkinetic and neuropathological parallels to indeterminate uric acid toxicity assume greater importance. The small, hard, painless, subcutaneous nodules attached to bones and tendons (a common symptom of many gout forms) may appear, indicating that the child's condition has become chronic. Chorea (St. Vitus' dance) is the most common manifestation of the neuropathological involvement of rheumatic fever, the connection between the two being universally recognized.

The symptoms of advanced uric acid toxicity, chorea and paralysis agitans, are so similar that a common etiological factor, uric acid, must be suspect. In all three of these conditions, speech, swallowing and locomotion suffer from muscular incoordination. The early, parallel symptoms of these pathologies are awkwardness and restlessness. Convulsive muscular movements usually show themselves first in an arm, a leg, or in the neck, and may remain localized. Just as in paralysis agitans, the child with fully developed chorea, when awake, is constantly twitching in the body, limbs, or face; when asleep, the neuropathological symptoms subside in either case. Generally, in these pathologies, the entire voluntary muscular system is deranged, while the involuntary muscles are scarcely affected. The rhythmic movements of the heart, for example, are not affected, but the heart may suffer impairment such as that which occurs in rheumatic stress.

Historically, the treatment of chorea follows the pattern of that observed in medicating rheumatism, hyperuricemia, paralysis agitans, and the various rheumatoid disorders, such as salicylates,

massage, gentle exercise, etc. Early treatment of chorea involved the use of arsenic and iron to act as alterants to the blood, since practitioners recognized the fact that a blood involvement existed.

In these blood involvements, it is of the utmost importance that blood toxins, such as uric acid, become suspect and that symptoms of nervousness, fatigue, and hyperkinetic disorders should not, as is commonly done, be attributed to a dietary or vitamin deficiency, or to a psychiatric pattern.

In rheumatic fever, subacute rheumatism, chronic rheumatism, muscular rheumatism and rheumatoid arthritis, the more effective medicaments are those compounds which have the property of lowering the uric acid and urate content of the body. These uricosuric agents include the salicylates, cincophen, carinamide, probenecid, ACTH and cortisone. Of these drugs, the salicylates have the comparative advantage of few side reactions and complications in the treatment of the pathologies of hyperuricemia. In the use of cincophen, argranulacytosis is common; carinamide is particularly toxic; probenecid slows some of the metabolic functions; while the use of ACTH and cortisone is limited by the general condition of the patient. Continued salicylate medication can have a depressing effect upon the patient for it can reduce the ascorbic acid reservoir of the tissues.

However, despite the fact that the body is not presumed to store vitamin C, the problem of ascorbic acid exhaustion is not a serious one since, in an absolute absence of vitamin C in the diet of a normal male, scorbutic symptoms will not appear for six to seven months.

Uric acid gives non-specific evidence of its accumulation in the tissues. These indications are not definitive, but it is important that they be recorded. They include: (1) the production, upon sneezing, of a particularly unpleasant odor; (2) the excessive accumulation of ear wax, apparently produced by the irritation of sodium biurate and uric acid which have a tendency to crystallize in the ears; (3) general fatigue.

More specific premonitory symptoms of hyperuricemia are found prior to an attack of ordinary gout. Among these are disorders of the digestive organs, capricious and feeble appetite, flatulence and pain, discomfort in the region of the liver and frequent micturition.

In irregular gout, articular tissues are not affected and the difficulty of diagnosis is that it may disturb the functions of various

organs. Regular gout, easily recognizable, is evidently the result of a long accumulation of sodium biurate rather than the uric acid; irregular gout is produced by a direct precipitation of the uric acid in the tissues at a time of extreme general physical and mental exertion. The symptoms of involvement of the tissues are not immediate and come about a week or ten days after exposure to the rigors of exertion. The first indication of this irregular uric acid toxicity is a constant swallowing which continues for about a week. This swallowing is the mucosa response of uric acid elimination. Fatigue now becomes evident, and there may be respiratory involvement which usually takes two forms. The ribs and intercostal muscles become affected by the inflammatory, irritant action of the uric acid deposited in their tissues. Then, histotoxic anoxia occurs; the oxygen supply is normal in every respect, but the degree of oxygen utilization is diminished by the presence of the excess uric acid in the blood and in the cells. Because of the anoxia, the patient responds with a greater respiratory effort for pulmonary ventilation, increased ammonia formation takes place in the kidney, increased acid secretion results, there is a general bodily diminution of electrolytes, and dehydration results.

Since these symptoms are so difficult to interpret, the patient generally maintains, within the limits of his discomfort, those dietary habits of high calorie, high purine protein diet and, usually, embarks on a vitamin program to correct fatigue or to sustain energy. This produces an autointoxication, a vicious circle of uric acid poisoning which eventuates in the neuropathological disorders previously noted.

During the period prior to the neurological involvements, hypoglycemia, to a minor degree, may manifest itself, the liver may become painful at times, and the blood pressure elevated. As the neurological symptoms approach, the arms and pulse are full and of high tension. This feeling extends to the shoulders and the neck. A great weakness overcomes the patient, his coordination becomes poor, particularly in walking, and there is a feeling of vertigo. This latter symptom has often resulted in a neurological diagnosis of an inner ear syndrome.

In the treatment of irregular gout, early diagnosis is important since the neurological involvements are more difficult to treat. At any stage of irregular gout, a severely limited caloric and protein diet is indicated. Purine must be eliminated completely, as well as the endogenic uric acid stimulants, such as liver extract and vita-

min B_{12}. Vitamin C should be eliminated and used only as it appears sparingly in foods. Vitamin B_1 intake should also be limited to that which is normal to ordinary food intake.

Phosphates and phosphoric acid should be included in the medication, since there is an apparent loss of these compounds during the development of the symptoms. It is likely that the uric acid usurps a site normally occupied by phosphoric acid in cell metabolism and it is important that the phosphates be present to replace the excess uric acid as the body gradually rids itself of it. Elixir Glycerophosphates Compound N. F., in doses of 4 cc. before each meal, is an ideal source of these phosphates and supplies the additional desirable stimulating effect of strychnine. Stimulants such as coffee, tea, or chocolate should be used in moderation since the caffeine and theobromine are purines which may evolve some uric acid.

Nicotinic acid is of great value in ameliorating the neuropathological and encephopathological symptoms. It should be used in quantities not exceeding 200 mg. per day, divided into four to eight doses.

Citrates may be used in the form of the potassium or sodium salt to hasten the removal of the uric acid, but the urine should be checked daily for an alkaline response. When this occurs, citrate medication should be suspended and should be reinstated only if the urine again becomes strongly acid.

It should also be noted that whiskey and brandy give temporary but marked relief to the extreme tensions of irregular gout and, if this is discovered by the patient and goes unchecked by the physician, may lead to alcoholism. The peripheral vasodilatory action of the nicotinic acid affords the same relief as alcohol. It should also be noted that avoidance of constipation is vital.

SUMMARY

In evaluating uric acid as an etiological factor in some of the obscure pathologies, this paper has indicated that: (1) the peculiar physico-chemical characteristics of uric acid place it in a position of pathological importance beyond that of the historically recognized disorders of gout and rheumatism, and their allied metabolic disturbances; (2) there is an evolutionary and hereditary factor involved, but that in modern societies of overproteinized and overvitaminized diets, none can be considered exempt from uric acid accumulation; (3) although children and women

are, to a degree, shielded from the disorders of uric acid accumulation, they too can be included among those who can be affected; (4) the more serious disorders resulting in neurological patterns of a hypokinetic nature are usually begun by an irregular or indeterminate form of gout; (5) this can produce a vicious circle of toxicity which leads to obscure neuropathologies; (6) uric acid toxicity is best controlled by limiting the intake of the purines and the metabolic stimulants that produce uric acid; (7) because of the nature of uric acid, it is difficult to dislodge it from the tissues and involves a long term of careful diet and of medication limited to the patient's restricted tolerance.

CONCLUSION

From the material contained in this study of uric acid, it can be seen that, in those cases of obscure origin in which the symptoms appear to be non-functional, subjective, psychosomatic, or hypertensive, it is important to determine the uric acid blood content, and that, if the content is abnormal or on the upper margin of the 2 mg. to 4 mg. per 100 cc. normality, the uric acid should be suspect as the etiological cause of the disorder.

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CONGENITAL ABSENCE OF THE SPLEEN. J. W. Murphy and W. A. Mitchell. (Pediatrics, 20:253-256, Aug. 1957). Congenital absence of the spleen was seen in a 15-month-old Negro female infant. Her condition was uncomplicated by other congenital abnormalities. The infant had a course marked by lack of resistance to infection and leukocyte counts so high as to simulate leukemia. The baby died with pneumonia and Waterhouse-Friderichsen syndrome. In most of the other reported patients splenic agenesis was associated with congenital cardiac anomalies, partial situs inversus, accessory lobe of the left lung, and abnormal mesenteric attachments. These anomalies probably arise from factors affecting the fetus at the 5-week stage of development. Some patients have hematological findings similar to post-splenectomy patients. The case reported is the eleventh in which splenic agenesis was the only congenital abnormality. —*J.A.M.A.*

HEMORRHAGIC COMPLICATIONS OF MEASLES

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Hemorrhagic skin manifestations are not uncommon in measles. As long as they are not associated with gross hemorrhage from other parts of the body with or without thrombocytopenia, they are not considered as complications and may be classified as severe variations of the ordinary type erythematous papular eruption of the disease to which the term ecchymotic measles has been applied by Griffith and Mitchell.[1] However, when hemorrhage is not confined to the skin but involves the mucous membrane of the gastro-intestinal tract, genito-urinary tract or central nervous system as well, the patient is usually critically ill and the mortality rate high. This type was designated malignant or black measles by the older writers.

Fortunately, this is a rare complication. From 1890 to date literature reveals only twenty-two well-documented cases.

The purpose of this paper is to add another case report and to discuss its unusual features.

CASE REPORT

The patient, an 8-year old, white female, was admitted to the Roosevelt Hospital, New York City, January 7, 1958, with a chief complaint of hematemesis. She was well until ten days prior to admission when she developed a sore throat, non-productive cough and a low-grade fever, for which she was treated with oral penicillin. Three days prior to admission, she developed a running nose and a temperature of 101°. Two days after the beginning of her illness, she vomited several tablespoons of bright red blood. On the day of admission, she again vomited approximately two cupfuls of coffee-ground material. At the same time she developed a rash over the face and trunk.

On admission, the patient was acutely ill and prostrated. Temperature was 104.2°. There was an erythematous, maculo-papular rash over the body and face. Coryza signs and Koplik spots were present. There were no petechiae and no ecchymoses at this time. Initial laboratory data revealed hemoglobin 13 grams, white blood

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count 12,800 with a differential of 90 per cent polymorphonuclears, 2 per cent lymphocytes, 8 per cent monocytes. Hematocrit was 36. Bleeding time was 1 minute 15 seconds and clotting time 5 minutes 35 seconds, capillary methods. Stool was 4 plus for guaiac.

Six hours after admission, the patient vomited about 150 ccs, of bright red blood with clots, but her vital signs remained stable. The second day of admission her temperature spiked to 105°. She was irrational. The maculo-papular rash became more generalized and confluent. The platelet count at this time was 100,000. The third day, the rash began to fade but on the back, lower part of the abdomen, and extremities it became hemorrhagic. This time the platelet count was 52,000, and the tourniquet test was strongly positive. She passed a tarry stool. Urinalysis was normal. The fourth day the temperature began to come down and her general condition improved considerably. Her platelet count rose to 126,000. The fifth day of hospitalization, her temperature was normal and remained so for the rest of her hospital stay, but there was crepitant rales heard over the left lower chest, posteriorly. However, chest x-ray was negative, and gastro-intestinal series was negative. She was placed on achromycin. The rest of her hospital stay was uneventful. She gradually improved. The hemorrhagic skin manifestations began to disappear. The platelet count rose to 382,000.

When she was discharged on January 17, 1958, physical examination was completely negative except for a fading hemorrhagic eruption.

DISCUSSION

Acute thrombocytopenia associated with hemorrhagic manifestation is encountered in other virus diseases besides measles. It occurs in smallpox[2], chickenpox[3], rubella[4], cat-scratch disease[5] and infectious hepatitis[6]. The pathogenesis of the bleeding tendency depends upon two factors: first, increased capillary fragility, which is due to direct damage to the capillary wall, a capillaritis[7].

These vascular lesions occur in the absence of thrombocytopenia and may cause death due to capillary damage alone. In fact, in an infant who died from extensive hemorrhage, an autopsy revealed hemorrhages throughout the gastro-intestinal tract but the platelet count and bleeding time were normal[8]. The second factor is acute thrombocytopenia. Perlman[9] has shown a tendency for the platelets to decrease during the different phases of uncomplicated

measles. There is no detailed information about the pathogenesis of the thrombocytopenia.

The comprehensive review of the literature by Hudson[10] showed that the time interval between the appearance of morbilliform rash and hemorrhagic manifestations is between two and fourteen days. In our case, gastro-intestinal bleeding developed *before* the appearance of the rash and during the episode of bleeding there were no hemorrhagic skin manifestations. The thrombocytopenia lasted for only four days. In most cases, the time interval before the platelets returned to normal is considerably longer than in the case here presented, in some instances up to three months[8]. At the height of the thrombocytopenia, there was no further gastro-intestinal bleeding in this case but hemorrhagic skin manifestations appeared at that time.

The degree of thrombocytopenia and increased capillary fragility probably do not depend upon the intensity of the infection but is related to the susceptibility of the individual patient's tissue.

The patient received no specific treatment. Very recently, Hudson has advocated the use of steroids and ACTH[10].

SUMMARY AND CONCLUSION

1. The case of severe gastro-intestinal hemorrhage, occurring in an 8-year old female with measles has been presented.

2. The mechanisms involved in the production of hemorrhage are discussed. It is probable that the extensive hemorrhage occurs either from capillary damage or from thrombocytopenia or both.

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DEPARTMENT OF ABSTRACTS

by

MICHAEL A. BRESCIA, M.D., NEW YORK

WEIR, H. F. AND ANDERSON, R. L.: ORGANIC AND ORGANIZATIONAL ASPECTS OF SCHOOL ADJUSTMENT PROBLEMS. (Journal American Medical Association, 166:1708, April 5, 1958).

In 181 school children with severe school adjustment problems, electroencephalographic and neurological evidence of brain damage was found in a large percentage of cases. The use of tranquilizing drugs to reduce the almost universal tension in these children was satisfactory. The diagnosis and treatment of school adjustment problems is not exclusively a medical problem but demands a working coordination of the private physician, the medical specialist, and the educational specialists in the school. When such coordination can be achieved, many children who now fail constantly in school and become a burden to the community in general may be rehabilitated and take a functional place in their society. The private physician should become a leader in this worthwhile project. AUTHORS' SUMMARY.

SUJOY, E. AND HALBERSTEIN, G.: POLIOMYELITIS IN THE CHILD UNDER A YEAR OF AGE. (Archivos Argentinos de Pediatria, 48:143, Sept. 1957).

The authors report on a study of 256 cases of acute anterior poliomyelitis in infants under one year of age. After a study of the literature they note that poliomyelitis in infants under a year of age is more common in their country than elsewhere. Of their cases fifty-five or 21 per cent occurred in infants under 6 months of age and the remainder between 6 and 12 months. The mortality rate is no different than other age groups. The main symptoms were fever, vomiting, angina, diarrhea and constipation. The spinal form occurred in 77.3 per cent, bulbo-spinal in 10.9 per cent and Landry's ascending type of paralysis occurred in 5.8 per cent of the cases. In one hundred and seventy-six cases (68.7 per cent) paralysis occurred one to five days after onset of illness, in thirty-seven (14.4 per cent) between 5 to 10 days and 10 to 30 days in the remainder. Various antibiotics were used without changing the course of the disease. M.A.B.

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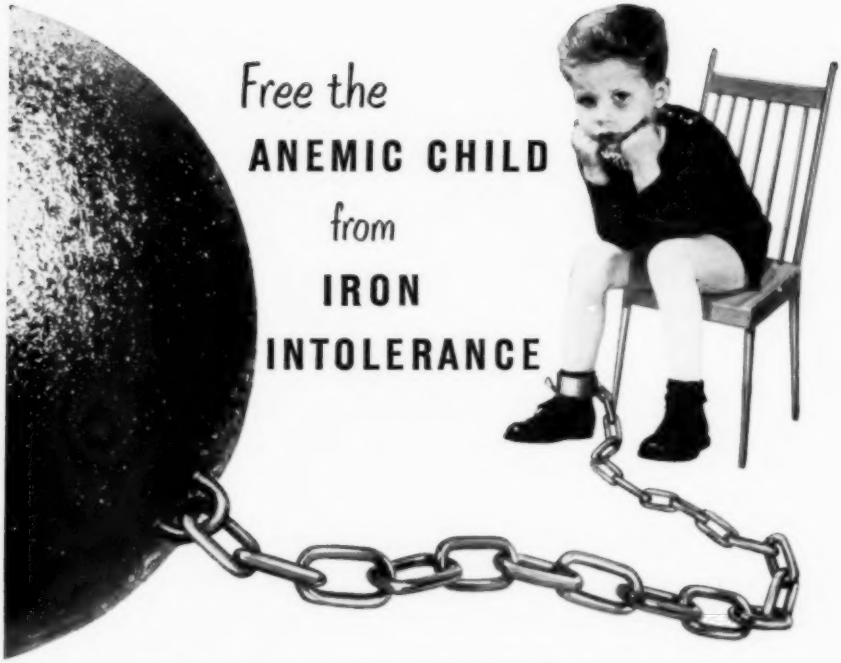

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